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Attorney's Docket No. 030560-03

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	)	
Andreas BERNKOP-SCHNURCH	)	Group Art Unit: 1619
Application No.: 09/830,986	)	Examiner: M. Willis
Filed: April 20, 2001	)	
For: MUCO-ADHESIVE POLYMERS,	)	
USE THEREOF AND METHOD FOR	)	
PRODUCING THE SAME	)	

DECLARATION

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

I, Andreas Bernkop-Schnurch, Ph.D., hereby declare as follows:

1. I am the named inventor for the above-identified application.
2. My Curriculum Vitae is attached hereto as Appendix A.
3. I am a person of at least ordinary skill in the art of mucoadhesives.
4. I have read the instant application as well as the Official Action dated March 27, 2002, and Constancis et al, U.S. Patent No. 5,496,872, which is cited therein.
5. I do not agree with the assertions in the Official Action that the instantly claimed invention is disclosed by or obvious in view of Constancis et al, U.S. Patent No. 5,496,872, or is obvious in view of Bernkop-Schnurch in combination with Constancis.
6. The instant invention relates to mucoadhesive polymers having improved properties. The improved mucoadhesive polymers "enable a targeted introduction of active substance in mucus layers, wherein a stable presence at the target site shall be enabled." By

this invention, an effective and efficient active substance delivery system is provided "by which an improved and thus also extended adhesion of drug on the mucosae can be attained." Page 2, ¶2, of the application.

7. The term "mucoadhesive" is recognized in the art. It is a term of art that is used to describe a particular class of polymers. U.S. Patent No. 5,047,244, for example, defines "mucoadhesive" as being "a material that adheres to a mucosal tissue surface in-vivo and/or in-vitro. Such adhesion will adherently localize the dosage form onto the mucus membrane and requires the application of a force of at least about 50 dynes/cm<sup>2</sup> to separate the mucoadhesive material from the mucus membrane." Col. 3, lns. 21-27.

8. The term "mucoadhesive," as used herein, is a polymer that adheres to the mucus layer covering a mucosal tissue surface in-vivo and/or in-vitro. Such adhesion has to be higher than at least 83 µJ for the total work of adhesion (TWA) described for tensile studies with dry compacts, according to Bernkop-Schnürch et al. *Pharm. Res.* 16, 1999, 876-881.

9. Mucoadhesive polymers are recognized in the art as including polyacrylates, (e.g., carbomer, polycarophil, carbopol, etc.), cellulose derivatives (e.g., sodium carboxymethylcellulose, hydroxypropylcellulose, etc.), hyaluronic acid, alginate, pectin and chitosan. See, e.g., Bernkop-Schnürch, A. (2002). *Mucoadhesive Polymers In: Polymeric Biomaterials* 2<sup>nd</sup> edition (Ed: Severian Dumitriu) Marcel Dekker, New York.

Hagerstrom H, Edsman K. "Interpretation of mucoadhesive properties of polymer gel preparations using a tensile strength method." *J Pharm Pharmacol* 2001 Dec; 53(12):1589-

Eouani C, Piccerelle P, Prinderre P, Bourret E, Joachim J. "In-vitro comparative study of buccal mucoadhesive performance of different polymeric films." *Eur J Pharm Biopharm* 2001 Jul; 52(1):45-55;

Singla AK, Chawla M, Singh A. "Potential applications of carbomer in oral mucoadhesive controlled drug delivery system: a review." *Drug Dev Ind Pharm* 2000 Sep; 26(9):913-24;

Kerec M, Bogataj M, Mugerle B, Gasperlin M, Mrhar A. "Mucoadhesion on pig vesical mucosa: influence of polycarbophil/calcium interactions." *Int J Pharm* 2002 Jul 8; 241(1):135-43;

Solomonidou D, Cremer K, Krumme M, Kreuter J. "Effect of carbomer concentration and degree of neutralization on the mucoadhesive properties of polymer films." *J Biomater Sci Polym Ed* 2001;12(11):1191-205;

Adriaens E, Remon JP, Ludwig A. "Evaluation of a mucoadhesive tablet for ocular use." Ceulemans J, Vermeire A, *J Control Release* 2001 Dec 13; 77(3):333-44;

Bernkop-Schnurch A, Gilge B., "Anionic mucoadhesive polymers as auxiliary agents for the peroral administration of (poly)peptide drugs: influence of the gastric juice." *Drug Dev Ind Pharm*. 2000 Feb; 26(2):107-13.

10. Constancis does not disclose or suggest "mucoadhesive" polymers, as instantly claimed. Constancis instead relates to "biocompatible and biodegradable surgical adhesives based on non-toxic products." Col. 1, lns. 39-42. More specifically, Constancis discloses biological "glues or gluing material." Col. 5, lns. 24-25. It is obvious that nobody would use

a surgical adhesive to try to connect one mucus gel layer with another, or to try to connect a mucus gel layer with a tissue.

11. The bioadhesives of Constancis are not "mucoadhesives." This would be apparent to a person skilled in the art. For example, Constancis' bioadhesives would not adhere to the mucosa with the same strength as a mucoadhesive polymer, for example, as taught by the '244 Patent. This is because they do not fulfill the minimal criteria to be mucoadhesive. For instance, in the teaching book *Drug Delivery Systems* (Ellis Horwood, New York), G. Hunt, P. Kearney and I. Kellaway defined criteria for polymers to be mucoadhesive in the chapter "Mucoadhesive polymers in drug delivery systems" as follows:

- Strong H-bonding groups (-OH, -COOH)
- Strong anionic charges
- Sufficient flexibility to penetrate the mucus network
- Surface tension characteristics suitable for wetting mucus/mucosal tissue surfaces
- High molecular weight

In contrast to the mucoadhesive polymers mentioned in ¶8 *supra* and also as claimed in my patent application, not even a single point out of these five is fulfilled by the monomers/polymers described by Constancis.

12. My invention relates to the surprising discovery that by introducing at least one non-terminal thiol group into a mucoadhesive polymer having not more than 10 different monomers, the mucoadhesive properties of the polymer are greatly improved. This discovery was unexpected. I discovered that the mucoadhesive polymers having the non-terminal thiol

group could form reversible, covalent bonds with the cysteine-rich subdomains of the mucus glycoproteins (see, Figure 1 of the application). These bonds allow for a stable localization of the polymers on the mucus layer of certain mucosal membranes. See also, page 3 of the application.

13. Unexpectedly, the mucoadhesive polymers of my invention have significantly improved binding capacity to intestinal mucosa. As stated *supra*, the most frequently used mucoadhesive polymers are polymers such as mentioned in claim 3 of the instant application, e.g., polyacrylates (Carbomer, Polycarbophil, Carbopol, etc.), cellulose derivatives (sodium carboxymethylcellulose, hydroxypropylcellulose, etc.), hyaluronic acid, alginate, pectin and chitosan.

14. In the following table the mucoadhesive properties of these polymers is listed. In addition, the improvement in the mucoadhesive properties of these polymers by the immobilization of thiol groups is shown as well.

Polymer	Total work of adhesion in $\mu\text{J}$ ; means $\pm$ SD (n= 3-8)	Reference
polycarbophil	110 $\pm$ 28	A. Bernkop-Schnürch, V. Schwarz, S. Steininger, Polymers with thiol groups: a new generation of mucoadhesive polymers? Pharm. Res. 16 (1999) 876-881.
thiolated polycarbophil	280 $\pm$ 68	
sodium carboxymethyl cellulose	108 $\pm$ 17	A. Bernkop-Schnürch, S. Steininger, Synthesis and characterisation of mucoadhesive thiolated polymers, Int. J. Pharm. 194 (2000) 239-247.

thiolated sodium carboxymethyl cellulose	157 $\pm$ 6	
chitosan HCl	23 $\pm$ 10	C.E. Kast, A. Bernkop-Schnürch, Thiolated polymers: development and in vitro evaluation of chitosan-thioglycolic acid conjugates, <i>Biomaterials</i> 22 (2001) 2345-2352.
thiolated chitosan	234 $\pm$ 0	
sodium alginate	26 $\pm$ 1	A. Bernkop-Schnürch, C.E. Kast, M.F. Richter, Improvement in the mucoadhesive properties of alginate by the covalent attachment of cysteine, <i>J. Control. Release</i> 71 (2001) 277-285.
thiolated sodium alginate	102 $\pm$ 36	

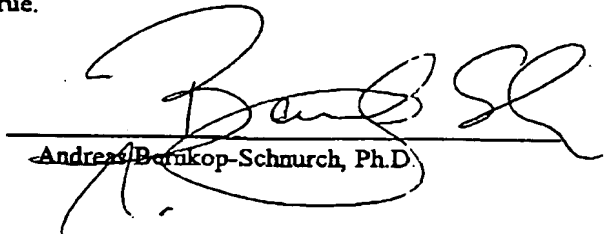
15. This strong improvement in the mucoadhesive properties was unexpected. It is based on thiol/disulfide exchange reactions between the polymer and the mucus layer. Prior to my invention, there was nothing reported in the literature about thiolated mucoadhesive polymers. This can be documented by the reviewer's report of the first publication submitted about thiolated mucoadhesive polymers. In the top-journal for this research field (*Pharmaceutical Research*) it is written about a "brilliant idea."

16. In addition, nothing is reported about this mechanism by Constancis et al.

17. I believe that the instant invention is truly novel. The improved properties of the mucoadhesive polymers I found were not suggested in the art generally, or more specifically in Constancis.

18. I further declare that I am aware that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and my jeopardize the validity of any patent application or any patent issuing thereon. All statements made of my own knowledge are true, and all statements made on information and belief are believed to be true.

28<sup>th</sup> August 2002  
Date

  
Andreas Demukop-Schmurch, Ph.D.

**Polymers with thiol groups: a new generation of mucoadhesive polymers?**

by Bernkop-Schnürch, Schwarz V, Steiniger S

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**General comments**

This is a well written article\* making use of the cleavage of disulfide bonds by compounds containing thiols as acetylcysteine. This well known reaction is exploited to increase unspecific mucoadhesion by cleaving the disulfide bridge of mucus with acetylcysteine coupled to polycarbophil with the result that polycarbophil is covalently linked to mucus. This idea is brilliant and there is some evidence given in the paper that it really works although the experimental in vitro circumstances especially if (synthetic) mucus is involved are very complex for a sound interpretation. The referee therefore suggests to include in this article simple ex-vivo methods as e.g. measuring of residence times of polymer-cysteine conjugates beads compared to polycarbophil beads in freshly isolated gut of rats or pigs as e.g. described by Lehr et al. in STP Pharma 5 (1989) 857-862 to have more evidence of improved mucoadhesion under physiological conditions.

Such a proof would also allow to omit the questionmark at the end of the title because then enough evidence is given that polymers containing thiol groups may be a new generation of mucoadhesive polymers if there are no toxicological constraints to use them.

\* (the English could be improved by the desk editor and there are some minor typing errors).



# Curriculum vitae

*Name:* Univ.-Prof. Dr. Andreas BERNKOP SCHNÜRCH

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*Born:* 1965 12 06 in Klagenfurt

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*Marital status:* single

May 2002	Offer for the Chair in Pharmaceutical Technology and Biopharmaceutics, Leopold-Franzens-Universität, Innsbruck
February 2002	First position in the ranking for the Chair in Pharmaceutical Technology and Biopharmaceutics, Leopold-Franzens-Universität, Innsbruck, Austria
April 2001	Offer for the C3-Professur, Institute of Pharmaceutical Technology and Biopharmaceutics, Ludwig-Maximilians-University, Munich, Germany
June 2000	Offer for the Chair in Pharmaceutics, School of Pharmacy, University of London
since March 1999	Associate Professor, permanent position at the Institute of Pharmaceutical Technology and Biopharmaceutics, University of Vienna
Nov. 1998	Habilitation for Pharmaceutical Technology, University of Vienna
April 1998	Second position in the ranking for the Chair in Pharmaceutical Technology and Biopharmaceutics (C4-Professor), Ludwig-Maximilians-University, Munich, Germany
May 1996	Proof of qualification for the wholesale trade of drugs
since 1994	Reader for: 'Peptide and Protein Drugs' 'Manufacturing of Cosmetics' and 'Manufacturing of Dosage Forms'
Oct. 1993 - May 1994	Military service
April 1994	Graduation as doctor for natural sciences at the University of Vienna
June 1991 - Oct. 1992	Scientific work at the Institute of Microbiology and Genetics, University of Vienna
since March 1991	Employment as 'University Assistant' at the Institute of Pharmaceutical Technology, University of Vienna
1990-1991	Practicing at a pharmacy in Vienna
Feb. 1990	Master degree at the University of Vienna
1984-1990	Study of pharmacy at the University of Vienna
1976-1984	Secondary school (Bundesgymnasium, St. Veit/Glan) -stress on natural science
1972-1976	Public primary school in St. Veit/Glan

## Andreas BERNKOP-SCHNÜRCH

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**Research field:** Development of drug delivery systems

(Poly)peptide drug delivery systems  
Enzyme-inhibitors as auxiliary agents  
Mucoadhesive polymers  
Permeation enhancement  
Sustained release systems  
Evaluation of drug absorption from mucosal tissues  
Evaluation of the presystemic metabolism of orally given drugs

### Original research articles

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1. Bernkop-Schnürch\*, A. (1997). Strategien zur peroralen Applikation von Peptid- und Proteinwirkstoffen. *Sci. Pharm.*, **65**, 61-81.
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3. Bernkop-Schnürch\*, A. (1998). The use of inhibitory agents to overcome the enzymatic barrier to perorally administered therapeutic peptides and proteins. *J. Control. Release*, **52**, 1-16.
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6. Bernkop-Schnürch\*, A. (2000). The Use of Multifunctional Polymers for the Noninvasive Peptide and Protein Application. *Expert Opinion Ther. Pat.* **10**, 1357-1366.
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### **Book Contributions:**

Bernkop-Schnürch\*, A. (2002). Mucoadhesive Polymers In: Polymeric Biomaterials: 2<sup>nd</sup> edition (Ed. Severian Dumitriu) Marcel Dekker, New York.

### **Patents:**

1. Bernkop-Schnürch, A. und Paikl, Ch. (1997). Verfahren zur Herstellung von Chitosan-Ethylendiamintetraacetat Konjugaten. AT Patentschrift 1997-01-21, A 79/97
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5. Bernkop-Schnürch, A., Schuhbauer, H. and Pischel, I. (1999).  $\alpha$ -Liponsäure(-Derivate) enthaltende Retardform, German patent application 1999-09-30; PCT-application pending.
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7. Bernkop-Schnürch, A. und Clausen, A. (2002). Drug delivery systems for the improvement of paracellular permeation of hydrophilic compounds. Austrian patent application.

### **Granted Projects:**

Bernkop-Schnürch, A.: Thiolisierte Polymere in Peptidwirkstoff-abgabesystemen, FWF-Project (Nov. 2001 – Sept. 2004; 300.000 Euro)

Bernkop-Schnürch, A.: Development of Drug Delivery Systems for the Peroral Administration of Peptide and Protein Drugs, FWF-Project (Jul. 1998 – Oct. 2001; 121,000 Euro)

Bernkop-Schnürch, A.: Development of Drug Carrier Systems with Improved Mucoadhesive Properties, FWF-Project (Nov. 1999 – Dec. 2002; 180,000 Euro)

Bernkop-Schnürch, A.: Entwicklung magensaftresistenter Arzneiformen für die perorale Applikation von Peptid- und Proteinwirkstoffen, Projekt der Hochschuljubiläumsstiftung der Stadt Wien (Jan. 1999 – Jun. 2000; 2,500 Euro)

Wugeditsch, Th., and Bernkop-Schnürch, A.: Entwicklung und Evaluierung von Ocularia basierend auf neuartigen mukoadhäsiven Polymeren, FWF-Impuls-Project (Aug. 2000 – Jul. 2002; 75,000 Euro)

Bernkop-Schnürch, A.: Thiolated Polymers in Peptide Drug Delivery Systems, FWF-Project (Nov. 2001 – Oct. 2004; 300,000 Euro)

Bernkop-Schnürch, A.: Der Einfluß von Thiolteilstrukturen auf die parazelluläre Permeation von Peptidwirkstoffen, *Projekt der Hochschuljubiläumsstiftung der Stadt Wien (Jan. 2002 – Jun. 2002; 2,100 Euro)*

### **Industrial Projects:**

Mucos Emulsionsgesellschaft, Leberstr. 96, A-1110 Vienna, Austria  
(*Development of oral protein delivery systems, Project leader: Mag. B. LOTZ*)

Degussa Trostberg, Dr.-A.-Frank-Str. 32, D-83308 Trostberg, Germany  
(*Development of sustained release systems for  $\alpha$ -lipoic acid, Project leader: Dr. H. SCHUHBAUER*)

Degussa Trostberg, Dr.-A.-Frank-Str. 32, D-83308 Trostberg, Germany  
(*Development of colon delivery system for  $\alpha$ -lipoic acid, Project leader: Dr. H. SCHUHBAUER*)

Croma-Pharma, Industriezeile 6, A-2100 Leobendorf, Austria  
(*Development of viscoelastic polymers for ophthalmic use, Project leader: Mag. M. PRINZ*)

Elan Pharmaceutical Technologies, Biotechnology Building, Trinity College, Dublin 2, Ireland  
(*Generation and evaluation of novel permeation enhancing systems, Project leader: Dr. A. RAOOF*)

Bayer AG, D-42096 Wuppertal, Germany  
(*Development of buccal delivery systems for peptide drugs, Project leader: Dr. J. KALBE*)

Bayer AG, D-42096 Wuppertal, Germany  
(*Development of a nasal delivery system for Vardenafil HCl, Project leader: Dr. J. KALBE*)

Serono, Istituto di Ricerca Cesare Serono SpA, Via di Valle Caia, 22 – 00040 –Ardea, Italy  
(*Development of Nasal Drug Delivery Systems for Beta Sheet Breaker Peptides, Project leader: Dr. Maria Dorly del CURTO*)

Serono, Istituto di Ricerca Cesare Serono SpA, Via di Valle Caia, 22 – 00040 –Ardea, Italy  
(*In vivo Evaluation of Different Oral Drug Delivery Systems for Antide, Project leader: Dr. Maria Dorly del CURTO*)

Trommsdorff GmbH & Co. KG, 52475 Alsdorf, Germany  
(Prüfung der mukoadhäsiven Eigenschaften von MTDA und MTDA-Lysinat,  
Project leader: Dr. Rudy SUSILO)

### **Collaborations:**

Univ. Prof. Dr. Udo M. Losert  
Institut für Biomedizinische Forschung  
Allgemeines Krankenhaus Wien / AKH Leitstelle 1Q  
Währinger Gürtel 18-20  
A-1090 Vienna, Austria  
(Tissue engineering by utilizing thiolated chitosans)

Univ. Prof. Dr. Rainer Oberbauer  
Univ.-Klinik für Innere Medizin III  
Abteilung von: Fachbereich Innere Medizin  
Währinger Gürtel 18-20  
A-1090 Vienna, Austria  
(Clinical studies with novel sustained release delivery systems)

Univ. Prof. Dr. Annick Ludwig  
Laboratory of Pharmaceutical Technology and Biopharmacy  
University of Antwerp, Universiteitsplein 1, B-2610 Antwerpen, Belgium  
(Development of ophthalmic drug delivery systems)

Dr. S. Senel  
Hacettepe University, Faculty of Pharmacy  
Department of Pharmaceutical Technology  
Ankara, Turkey  
(The use of thiolated chitosan in buccal delivery systems)

Univ. Prof. Dr. Paolo Caliceti  
Department of Pharmaceutical Sciences  
Faculty of Pharmacy  
University of Padua  
Via F. Marzolo, 535131 Padua - Italy  
(Development of oral insulin delivery systems)

Univ. Prof. Dr. Ivo Schmerold  
Veterinärmedizinische Universität Wien  
Institut für Pharmakologie und Toxikologie  
Veterinärplatz 1  
A - 1020 Vienna, Austria  
(Evaluation of mucoadhesive delivery systems in pigs)

Dr. Alexander Becherer  
Univ.-Klinik für Nuklearmedizin  
Allgemeines Krankenhaus Wien / AKH Leitstelle 1Q

Währinger Gürtel 18-20

A-1090 Vienna, Austria

*(Szintigraphic determination of the GI-transit time of mucoadhesive delivery systems in human volunteers)*

### **Prizes awarded:**

*HERBA-Award 1997 (3,000 Euro)*

*Research-Award of the City of Vienna 1999 (3,000 Euro)*

*Eurand-Award 2000 (1,500 Euro)*

*Best of Biotech Award 2001 Phase I (725 Euro)*

*Best of Biotech Award 2001 Phase II (1,450 Euro)*

*MBPW Award 2002 Phase I-III (26,750 Euro)*

### **Oral Presentations:**

Bernkop-Schnürch, A. (1991) The Use of *Escherichia coli* Adhesive Antigen K99 for Drug Carrier Systems. Institute of Microbiology and Genetic, University of Vienna.

Bernkop-Schnürch, A. (1992) Searching for Peptide Ligands with an Epitope Library. Institute of Microbiology and Genetic, University of Vienna.

Bernkop-Schnürch, A. (1995) Ansätze zu peroralen (Poly)peptid Applikationssystemen. Institute of Pharmaceutical Technology, University of Vienna.

Bernkop-Schnürch, A. (1996) Entwicklung eines bioadhesiven Arzneistoffabgabesystems zur peroralen Ulkustherapie mittels EGF. Institute of Pharmaceutical Technology, University of Vienna.

Bernkop-Schnürch, A. (1997) Enzyminhibitoren als Hilfsstoffe zur peroralen Applikation von Peptid- und Proteinwirkstoffen. ÖPHG Congress, Vienna.

Bernkop-Schnürch, A. (1997) Strategien zur peroralen Applikation von Peptid- und Proteinwirkstoffen. HERBA-Award, Vienna.

Bernkop-Schnürch, A. (1997) Strategies for the peroral administration of insulin. Institute of Pharmaceutical Chemistry, University of Padova, Italy.

Bernkop-Schnürch, A. (1997) Intestinal peptide and protein delivery: Coadministration of inhibitory agents. 2nd Central European Symposium on Pharmaceutical Technology, Portoroz, Slovenia.

Bernkop-Schnürch, A. (1998) Development of drug delivery systems with protective effect towards GI proteases. 2nd World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology, Paris, France.

Bernkop-Schnürch, A. (1998) Entwicklung bioadhäsiver Polymere zur peroralen Applikation von Peptid- und Proteinwirkstoffen, Ludwig Maximilians Universität Munich, Germany.

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Bernkop-Schnürch, A. (1998) Synthese von Polymeren zur peroralen Applikation von Peptid- und Proteinwirkstoffen, AKH Vienna.

Bernkop-Schnürch, A., Schwarz, V., and Thaler, S. (1999) Improved Mucoadhesive Properties of Polycarbophil by the Covalent Attachment of Cysteine, 26th Int. Symp. on Controlled Release of Bioact. Mat., Boston, USA.

Bernkop-Schnürch, A. (1999) Thiolated polymers: a new generation of mucoadhesive polymers, 3rd Central European Symposium on Pharmaceutical Technology, Portoroz, Slovenia.

Bernkop-Schnürch, A. (1999) Enzyme-Inhibitors, Elan Pharmaceutical Technologies, Dublin, Ireland.

Bernkop-Schnürch, A. (1999) Novel Delivery Systems for alpha-Lipoic Acid, 2nd Dietary Supplement Symposium Trostberg, Germany

Bernkop-Schnürch, A., Marschütz, M. and Clausen, A. (2000) Design of Polymeric Conjugates for Improved Oral Delivery, 4th International Symposium on Polymer Therapeutics, University of London, London, U.K.

Bernkop-Schnürch, A. (2000) The Use of Thiolated Polymers in Oral Drug Delivery, 27th Int. Symp. on Controlled Release of Bioact. Mat., Paris, France.

Bernkop-Schnürch, A. (2000) Polymeric Conjugates in Oral Drug Delivery – An Overview, Elan Pharmaceutical Technologies, Dublin, Ireland.

Bernkop-Schnürch, A. (2000) New Approaches in the Development of Drug Delivery Systems, Cardiff, UK.

Bernkop-Schnürch, A. (2000) Thiolated (Poly)acrylates, CPhI Congress, Milano, Italy.

Bernkop-Schnürch, A. (2000) Der Einsatz chemisch modifizierter Polymere als Wirkstoffträgermatrix, München, Deutschland

Bernkop-Schnürch, A. (2001) Das LADME Prinzip aus Pharmazeutisch Technologischer Sicht, Institute of Pharmaceutical Chemistry, Vienna, Austria

Bernkop-Schnürch, A. (2001) Thiolated Polymers: A New Platform Technology for Drug Delivery Systems? Serono, Turin, Italy

Bernkop-Schnürch, A. (2001) Thiomere: Eine neue Generation polymerer Hilfsstoffe, Jena, Germany

Kast C., Hornof M. and Bernkop-Schnürch A., (2001) Einfluß von kovalent gebundenen Thiolgruppen auf die mukoadhäsiven und viskoelastischen Eigenschaften von Chitosan. 6. Österreichischer Kohlenhydratworkshop, Vienna, Austria

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## **Poster Presentations:**



Bernkop-Schnürch, A., Gabor, F., Szostak, M. und Lubitz, W. (1992) Gentechnologische Herstellung Bioadhäsiver Arzneistoffträger. ÖPHG Congress, Vienna.

Bernkop-Schnürch, A., Gabor, F. und Spiegl, P. (1995) Bioadhäsiva: Isolierung und Charakterisierung von *E. coli* K99 Fimbrien. ÖPHG Congress, Innsbruck, Austria.

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Bernkop-Schnürch, A., and Pasta, M. (1998) Intestinal Peptide and Protein Delivery: Synthesis and Evaluation of Chitosan-EDTA - Bowman-Birk Inhibitor Conjugates. The 17th Pharmaceutical Technology Conference and Exhibition, Dublin, Ireland.

Bernkop-Schnürch, A., Humenberger, C., and Valenta, C. (1998) Influence of Ionic Crosslinkers on Cohesiveness of Bioadhesive Polymers used as (Poly)peptide Drug Carrier Matrices. The 17th Pharmaceutical Technology Conference and Exhibition, Dublin, Ireland.

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Clausen, A., Marschütz, M., Riegler, M. and Bernkop-Schnürch, A. (1999) Thiolated polycarbophil as penetration enhancer for (poly)peptide drugs, 26th Int. Symp. on Controlled Release of Bioact. Mat., Boston, USA.

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Clausen, A., Marschütz, M., Steininger, S. and Bernkop-Schnürch, A. (1999) Method to control the stability of matrix tablets based on thiolated polycarbophil, 3rd Central European Symposium on Pharmaceutical Technology, Portoroz, Slovenia

Bernkop-Schnürch, A., Hoffer, M., Kirchmayer, R. and Kratzel, M. (1999) A drug delivery system with protective effect towards pepsinic degradation - development, synthesis and *in vitro* evaluation, 3rd Central European Symposium on Pharmaceutical Technology, Portoroz, Slovenia

Marschütz, M., Clausen, A., and Bernkop-Schnürch, A. (1999) Development of a CMC-inhibitor conjugate protecting insulin from enzymatic attack in an artificial intestinal fluid, 3rd Central European Symposium on Pharmaceutical Technology, Portoroz, Slovenia

Kratzel, M., and Bernkop-Schnürch, A. (1999) Valaminole—neue simplifizierte Pepstatin A—Analoge: Synthese und Evaluierung als Pepsin-Inhibitoren, ÖPHG-Tagung, Innsbruck, Austria

Clausen, A.E., Marschütz, M., Kast, C., Freudl, J. and Bernkop-Schnürch, A. (2000) Design and *in vitro* Evaluation of a Drug Carrier Matrix Based on a Thiolated Polymer, Bioencapsulation: Innovation and Technologies, Vienna, Austria

Clausen, A.E., Marschütz, M. and Bernkop-Schnürch, A. (2000) Permeation Enhancing Effect of Thiolated Carboxymethylcellulose, 27th Int. Symp. on Controlled Release of Bioact. Mat., Paris, France.

Freudl, J., Clausen, A.E. and Bernkop-Schnürch, A. (2000) Thiolated Polycarbophil: A Promising Enhancer for the Paracellular Route of Drug Absorption? 27th Int. Symp. on Controlled Release of Bioact. Mat., Paris, France.

Kast, C.E., Freudl, J. and Bernkop-Schnürch, A. (2000) Mucoadhesive Thiolated Polymers: Synthesis and *in vitro* Evaluation of Chitosan-Thioglycolic Acid Conjugates, 27th Int. Symp. on Controlled Release of Bioact. Mat., Paris, France.

Marschütz, M.K., Caliceti, P., Clausen, A.E. and Bernkop-Schnürch, A. (2000) Design and *in vivo* Evaluation of an oral Delivery System for Insulin, 27th Int. Symp. on Controlled Release of Bioact. Mat., Paris, France.

Bernkop-Schnürch, A., Clausen, A.E. and Kast, C.E. (2000) Stabilization of Polymeric Drug Carrier Systems via Disulfide Bond Formation, 27th Int. Symp. on Controlled Release of Bioact. Mat., Paris, France.

Bernkop-Schnürch, A., Clausen, A.E. and Kast, C.E. (2000) The Use of Thiomers as Multifunctional Excipients in Drug Delivery, 10<sup>th</sup> Internat. Pharm. Technol. Symposium, Istanbul, Turkey.

Clausen, A.E., Hnatyszyn, M., Kast, C.E., Marschütz, M.K., and Bernkop-Schnürch, A. (2000) Thiolated carboxymethylcellulose: a new excipient for enhanced hydrophylic therapeutic absorption. 10<sup>th</sup> Internat. Pharm. Technol. Symposium, Istanbul, Turkey.

Kast, C.E., Clausen, A.E., Marschütz, M.K., Bernkop-Schnürch, A. (2000) Biodegradation of chitosan-thioglycolic acid conjugates by lysozyme. 10<sup>th</sup> Internat. Pharm. Technol. Symposium, Istanbul, Turkey.

Marschütz, M.K., Veronese, F.M., Clausen, A.E., and Bernkop-Schnürch, A. (2000) Synthesis and *in vitro* evaluation of a polycarbophil-PEG-

inhibitor conjugate—a novel excipient for oral peptide drug delivery?. 10<sup>th</sup> Internat. Pharm. Technol. Symposium, Istanbul, Turkey.

Kast C. and Bernkop-Schnürch A. (2001) Synthesis and in vitro evaluation of polycarbophil-cysteamine conjugates. 4th Central European Symposium on Pharmaceutical Technology, Vienna, Austria.

Kast C., Senel S., Özalp M., Hincal A., Hornof M. and Bernkop-Schnürch A. (2001) Antimicrobial activity of chitosan-thioglycolic acid conjugates. 4th Central European Symposium on Pharmaceutical Technology, Vienna, Austria.

Langoth N., Walker G. and Bernkop-Schnürch A. (2001) Aminopeptidase activity on the surface of the porcine buccal mucosa. 4th Central European Symposium on Pharmaceutical Technology, Vienna, Austria.

Marschütz M. and Bernkop-Schnürch A. (2001) Interaction of a poly(acrylic acid)-cysteine conjugate with the intestinal mucus gel layer. 4th Central European Symposium on Pharmaceutical Technology, Vienna, Austria.

Walker G., Langoth N. and Bernkop-Schnürch A. (2001) A new in vitro system for measuring the metabolic barrier of the buccal epithelium. 4th Central European Symposium on Pharmaceutical Technology, Vienna, Austria.

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Scientia Pharmaceutica  
Biomacromolecules